

ODM and Methidathion Technical Briefing

December 8, 1999
Sacramento, California



Overview

Lois Rossi, Director
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OPP

Overview of Day's Activities

- Legal framework and regulatory history
- Provide usage profiles
- Present risk assessments
- Questions and comments

Goals of Meeting

- Provide an understanding of EPA's risk assessments
- Answer your questions
- Identify risks of concern
- Begin risk mitigation dialog

Legal Context

FQPA amendments to FIFRA required:

- Reassessment of all existing tolerances
- Aggregate assessments
- Safety factor for children
- Cumulative assessments

EPA Implementation of FQPA

- Formation of Tolerance Reassessment Advisory Committee (TRAC)
- Development of science policies
- Development of pilot process for public participation
- Focus on OPs

TRAC Pilot OP Review Process

- Phase 1 (30 days)
 - Registrant "Error Only" Review
- Phase 2 (up to 30 days)
 - EPA considers registrants' comments
- Phase 3 (60 days)
 - Public comment on preliminary risk assessment

TRAC Pilot OP Review Process

- Phase 4 (90 days)
 - EPA revises risk assessments, holds public meetings/technical briefings
- **Phase 5 (60 days)**
 - **EPA solicits risk management ideas**
- Phase 6 (up to 60 days)
 - EPA develops risk management strategies

Regulatory History

Michael Goodis, Chemical Review Manager
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ODM: Phase 3 - Public Comments

- Comments received from registrant, growers, and public
- Registrant's concerns
 - 10X FQPA Safety Factor (SF)
 - Intermediate-term exposure assessment for handlers
 - Postapplication assessment
 - Assumptions/defaults used in ecological risk assessments

ODM: Phase 3 - Public Comments

- Agricultural Extension Office (Oregon) provided information on alfalfa use
- Grower comments
 - Importance for IPM programs
 - No equivalent alternatives
 - Use of actual rather than “theoretical” data
 - Safe for field workers

ODM: Phase 4 - Revise Assessments

- New toxicity data received
 - Relieved concern about heritable effects
- FQPA SF reduced to 1X
- Refinement of dietary assessment
- Revisions to worker risk assessment
 - Update use rate for some crops
- Drinking water assessment refined

Methidathion: Phase 3 - Public Comments

Comments received from:

- Registrants
- Growers
- Grower groups
- Other governmental agencies - state and local

Methidathion: Phase 3 - Public Comments

- Continued use - artichokes
- Important IPM tool
- Limited effective alternatives
- Products are safe for field workers

Methidathion: Phase 4 - Revise Risk Assessments

Changes to risk assessments

- Refined acute dietary assessment
- Dermal toxicity endpoint selection
- Revised worker exposures
 - Handlers
 - Harvesters

Generic Phase 3 - Public Comments

Natural Resources Defense Council (NRDC) - comments for all OPs

- Common mechanisms
- FQPA 10X Safety Factor
- Highly exposed populations
- Data requirements/assumptions
- Transitioning to safer alternatives

ODM: Regulatory History

- First registered in 1961 by Mobay Chemical Co.
- Registration Standard issued 1987
- In 1994, registration transferred to Gowan Co.

ODM: Regulatory History

- Special Review initiated in 1987
 - Concern about reproductive effects
 - Reviewed data to clarify reproductive toxicity
 - Reproductive effects at higher doses than ChEI
 - Close out at same time as reregistration

ODM: Regulatory History

- 1994 settlement agreement with Gowan Co.
 - Interim measures to protect workers
 - Special Review risk concerns
 - 9 uses removed from end-use labels
 - Provision to be reinstated
 - Uses included in risk assessment

ODM: Regulatory History

- Proposition 65 - ODM listed
 - Reproductive toxicity
 - Listed in November 1998
- Minimum exposure pesticide
 - Requires specific worker protective measures - PPE and engineering controls

Methidathion: Regulatory History

- First registered in 1972 by Ciba-Geigy
- Registrants are Novartis and Gowan Co.
- Registration Standard issued in 1983 and revised and reissued in 1988
- In July 1998, methidathion presented to TRAC as case study

Use Profile

Don Atwood, Entomologist
Biological & Economic Analysis Division
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ODM: Use Profile

- Restricted use organophosphate class insecticide-miticide
- Mode of action
 - Acetylcholine esterase inhibition
- Registered uses
 - Field crops, non-bearing fruit, vegetables, melons, nuts
 - Additional use on Christmas trees, seed orchard trees, ornamentals
- Average domestic use 1987-1997
 - 154,000 lbs ai on 231,000 acres

ODM: Use Profile

Use Practices

- Formulations
 - Spray concentrate (Metasystox R) - 25% ai
 - Ready-to-use liquid for tree injection (Harpoon, Inject-A-Cide) - 50% ai
- Use Rates
 - 0.375 - 1.125 lbs ai/acre
 - 1-3 applications per season
 - Most acreage treated with 1 lb ai or less per application year

ODM: Use Profile

Use Practices (cont.)

- Application Methods
 - Aerial (fixed-wing or helicopter)
 - Airblast sprayer
 - Groundboom sprayer
 - Bark treatment (brush on or inject)
 - Chemigation
 - Soil injection

ODM: Use Profile

Usage

- Major use sites (% total lbs ai)
 - Broccoli (29.9%)
 - Cauliflower (14.2%)
 - Mint (10.4%)
- Major use sites (% crop treated)
 - Broccoli (62%)
 - Cauliflower (46%)
 - Brussels sprouts (75%)
 - Mint (12%)
 - Alfalfa seed (11%)

ODM: Use Profile

9 use sites were included in the analysis,
but were dropped from the marketing
label (1994)

- Citrus
- Field corn
- Onions
- Pears
- Popcorn
- Safflower
- Snap bean
- Sorghum
- Turnip

ODM: Use Profile

Four uses have been canceled and were
not included in the analysis

- Raspberry
- Blackberry
- Potato
- Pea

Methidathion: Use Profile

- Organophosphate insecticide-miticide
- Mode of action
 - Acetylcholine esterase inhibition
- Registered uses
 - Field crop, vegetable crop, fruit crop, nut crop
- Average domestic use 1987-1997
241,000 lbs ai on 138,000 acres

Methidathion: Use Profile

- 4 end-use products
- Supracide (22.6% emulsifiable concentrate)
 - Supracide 2E (24.4% emulsifiable concentrate)
 - Supracide 25WP (25% wettable powder)
 - Supracide W (25% wettable powder)

Methidathion: Use Profile

- Application Methods
 - aircraft
 - ground sprayer (low and high volume)
 - hand-held sprayer
- Use Rates
 - Average application rate: 0.4-2.8 lbs ai
 - Average number of applications: 1-2.5 times per season
 - Most acreage treated with 2.8 lbs ai or less per application year

Methidathion: Use Profile

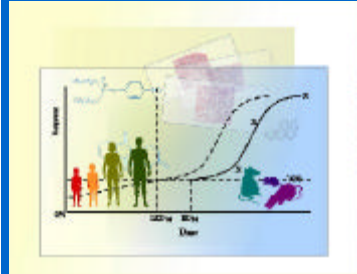
- Major use sites (% total lbs ai)
 - Almonds (18%)
 - Oranges (17%)
 - Plums & prunes (15%)
 - Walnuts (13%)
- Major use sites (% acres treated)
 - Artichokes (50%)
 - Plums & prunes (11%)
 - Walnuts (9%)

Methidathion: Use Profile

Sources of Data

- USDA/NASS
- California Department of Pesticide Regulation
- National Center for Food and Agricultural Policy
- Gowan and Novartis
- Proprietary EPA databases

Human Health Risk Assessment



www.epa.gov/pesticides/op/ODM.htm
www.epa.gov/pesticides/op/methidathion.htm

Human Health Risk Assessments Overview

Jess Rowland, Branch Chief
Health Effects Division
OPP

Risk Assessment Components

- Dietary
 - Food
 - Drinking water
- Occupational
 - Handlers/applicators
 - Workers (postapplication)
- Aggregate (food, drinking water)

Basic Risk Equation

$$\text{Risk} = \text{Hazard} \times \text{Exposure}$$

Occupational Risk Assessments

- Handlers
 - Mixers
 - Loaders
 - Applicators
- Postapplication workers

Occupational Risk Assessments

Duration of Exposure Route of Exposure

- Short-term
 - Intermediate-term
 - Long-term
- Dermal
 - Inhalation

Hazard Identification Process

- Review/evaluation of all toxicology studies
- Selection of studies appropriate for route and duration
- Simulate actual exposure conditions

Hazard Identification Process

- Consider all adverse effects seen
- Selection of critical endpoint of concern
- Selection of the lowest NOAEL for the critical effect
- Dose/endpoint selected would be protective of all adverse effects

Effect Levels

- Lowest Observed Adverse Effect Level = LOAEL
 - The lowest dose at which an “adverse” health effect is seen. Has units of mg per kg body weight per day.
- No Observed Adverse Effect Level = NOAEL
 - The dose at which no “adverse” health effect is seen. This dose is less than the LOAEL. Has units of mg per kg body weight per day.

Uncertainty and Safety Factors

- 10X Interspecies Extrapolation
 - 10X Intraspecies Variation
 - 1X to 10X FQPA Safety Factor
-
- 100X to 1000X Total Uncertainty and Safety Factors for Risk Assessment

Expression of Occupational Risk

$$\text{MOE} = \frac{\text{NOAEL}}{\text{Exposure}}$$

- Generally, an MOE of 100 or greater is protective
- The larger the MOE, the lesser the concern

Hazard Identification for Occupational Risk Assessment

ODM: Occupational Risk Assessments

- Short-term exposure = 1 to 7 days
 - Short-term dermal dose:
 - NOAEL of 5.0 mg/kg/day
 - Target MOE: 100
 - Inhalation dose:
 - LOAEL of 17 mg/kg/day
 - Target MOE: 300

ODM: Occupational Risk Assessments

- Intermediate-term exposure = 7 days to several months
 - Intermediate-term dermal dose:
 - NOAEL of 0.3 mg/kg/day
 - Target MOE: 100
 - Inhalation dose:
 - LOAEL of 17 mg/kg/day
 - Target MOE: 300

Methidathion: Occupational Risk Assessment

- Short-term exposure
 - Study: 21-day dermal - rabbit
 - Dose: NOAEL: 20 mg/kg/day
 - Target MOE: 100

Methidathion: Occupational Risk Assessment

- Intermediate-term exposure
 - Study: 90-day neurotoxicity - rat
 - Dose: NOAEL: 0.2 mg/kg/day
 - Dermal absorption: 30%
 - Target MOE: 100

Methidathion: Occupational Risk Assessment

- Inhalation exposure
 - Study: 90-day neurotoxicity - rat
 - Dose: NOAEL: 0.2 mg/kg/day

ODM: Occupational Risk Assessment

Kelly O'Rourke, Occupational Risk Assessor
Health Effects Division
OPP

ODM: Occupational Risk Assessment

Handlers

- Professional pesticide applicators and farmers/growers who mix, load and apply pesticides

Post-Application Workers

- Workers who irrigate, sort and pack, hand harvest, stake/tie, transplant, ball/burlap

ODM: Occupational Handler Risk Assessments

Handler Risk Factors

- Formulation, activity, and application equipment
- Levels of protection
- Rate of application
- Area treated
- Toxicity endpoint

ODM: Occupational Handler Risk Assessments

Handler Risk

$$\text{Dose} = \frac{\text{UE} \times \text{App Rate} \times \text{Acres Treated}}{\text{Body Weight}}$$

$$\text{MOE} = \frac{\text{NOAEL or LOAEL}}{\text{Dose}}$$

ODM: Occupational Handler Risk Assessments

- Short-term exposure = 1 to 7 days
 - Short-term dermal endpoint:
 - NOAEL of 5.0 mg/kg/day
 - Target MOE: 100
 - Inhalation endpoint:
 - LOAEL of 17 mg/kg/day
 - Target MOE: 300

ODM: Occupational Handler Risk Assessments

- Intermediate-term exposure > 7 days to several months
 - Dermal endpoint:
 - NOAEL of 0.3 mg/kg/day
 - Target MOE: 100
 - Inhalation endpoint:
 - LOAEL of 17 mg/kg/day
 - Target MOE: 300

ODM: Occupational Handler Risk Assessments

Handler Scenarios: Agricultural

- Mixer/Loader (M/L) - Liquids
 - Aerial
 - Chemigation
 - Groundboom
 - Airblast sprayer
 - High-pressure wand

ODM: Occupational Handler Risk Assessments

Handler Scenarios: Agriculture

- Applicators - Liquids
 - Aerial
 - Groundboom
 - Airblast
 - High-pressure wand
 - Tree injection

ODM: Occupational Handler Risk Assessments

Handler Scenarios: Agriculture

- Mixer/Loader/Applicator (M/L/A) - Liquids
 - Low-pressure handwand
 - Backpack sprayer
 - Soil injection (ornamental - not ag)
 - Paintbrush (ornamental - not ag)
- Flagger
 - Aerial

ODM: Occupational Handler Risk Assessments

Data Gaps

- 2 scenarios lacking exposure data; no quantitative assessment
 - Applications for tree injection (ready-to-use liquids)
 - Mixing/loading/applying liquids using soil injection

ODM: Occupational Handler Risk Assessments

Pesticide Handlers Exposure Database

- Developed by Task Force
- Monitored exposure data
- Consistency
- Widely accepted

ODM: Occupational Handler Risk Assessments

Current labels require:

- Long-sleeved shirt
- Long pants
- Coveralls
- Chemical-resistant gloves
- Chemical-resistant footwear and socks
- Chemical-resistant headgear
- Chemical-resistant apron
- Respirator

ODM: Occupational Handler Risk Assessments

Current labels (cont.)

- Closed mixing/loading for aerial and chemigation
- Enclosed cab truck for flaggers

ODM: Occupational Handler Risk Assessments

Handler Results: Inhalation

- Label requires respirator
- MOEs range from 1,000 to >300,000 with respirator
- Inhalation not of concern for any scenario
- Target MOE = 300

ODM: Occupational Handler Risk Assessment

Handler Results: Dermal

- Short-term handler risks
 - 4 scenarios do not reach the target MOE
- Intermediate-term handler risks
 - 10 scenarios do not reach the target MOE
- Target MOE = 100

ODM: Occupational Handler Risk Assessment

Aerial and Chemigation ¹	Range of MOEs (Dermal)	
	PPE ²	Engineering Controls ³
Mixer/Loader (M/L)	3.5 – 9.4	7.0 - 19⁴
Applicator (A)	Not feasible	16 - 63
Flagger (F)	8.0 - 12	360 - 550⁴

¹Intermediate-term; dermal route; 350 acres treated; A & F not applicable for chemigation

²Double layer clothing, chemical-resistant gloves (M/L); double layer clothing (F)

³Closed system, single layer clothing, chemical-resistant gloves (M/L); closed cockpit/cab, single layer clothing, no gloves (A, F)

⁴Bolded values represent best data match to current label requirement.

ODM: Occupational Handler Risk Assessment

Groundboom ¹	Range of MOEs (Dermal)	
	PPE ²	Engineering Controls ³
Mixer/Loader (M/L)	15 – 41 ⁴	31 - 81
Applicator (A)	32 – 48 ⁴	70 - 110

¹ Intermediate-term; dermal route; 80 acres treated

² Double layer clothing, chemical-resistant gloves (M/L, A)

³ Closed system, single layer clothing, chemical-resistant gloves (M/L); closed cockpit/cab, single layer clothing, no gloves (A)

⁴ Bolded values represent best data match to current label requirements.

ODM: Occupational Handler Risk Assessment

Airblast ¹	Range of MOEs (Dermal)	
	PPE ²	Engineering Controls ³
Mixer/Loader (M/L)	55 - 82 ⁴	95 - 160
Applicator (A)	4.2 – 6.4 ⁴	49 - 74

¹ Intermediate-term; dermal route; 25-40 acres treated

² Double layer clothing, chemical-resistant gloves (M/L, A)

³ Closed system, single layer clothing, chemical-resistant gloves (M/L); closed cockpit/cab, single layer clothing, chemical-resistant gloves (A)

⁴ Bolded values represent best data match to current label requirements.

ODM: Occupational Handler Risk Assessment

Handwand Backpack Sprayer Paintbrush ¹	Range of MOEs (Dermal)	
	PPE ²	Engineering Controls ³
Mixer/Loader (M/L)	55 – 920⁴	95 – 1,800
Applicator (A)	2.6 – 43⁴	Not feasible
Mixer/Loader/ Applicator (M/L/A)	0.048 – 73⁴	Not feasible

¹Short- & intermediate-term; dermal route; 20 acres treated for M/L, A; 5-40 gallons for M/L/A

²Double layer clothing, chemical-resistant gloves (M/L)

³Closed system, single layer clothing, chemical-resistant gloves (M/L)

⁴Bolded values represent best data match to current label requirements.

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ODM: Occupational Postapplication Risk Assessment

Postapplication Worker Risk

- Dislodgeable Foliar Residue (DFR)
 - Amount of residue that workers could contact in field
- Transfer Coefficient (TC)
 - Indicator of amount that workers actually contact during various field activities

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ODM: Occupational Postapplication Risk Assessment

Post-Application Worker Risk Calculation

$$\text{Dose} = \frac{\text{DFR} \times \text{TC} \times \text{hours worked}}{\text{body weight}}$$

$$\text{MOE} = \frac{\text{NOAEL}}{\text{Dose}}$$

ODM: Occupational Postapplication Risk Assessment

Sources of Information

- DFR Data
 - Registrant-submitted studies on cauliflower, bell pepper, cotton and sugar beets
 - Cauliflower data - surrogate for other cole crops
 - Bell pepper data - surrogate for eggplant
 - Remaining crops were assessed using average residue data from the 4 crops studied

ODM: Occupational Postapplication Risk Assessments

Sources of Information (cont.)

- Transfer Coefficients
 - Standard values, based on historical data
 - Crops with DFR data were assessed individually
 - Crops lacking their own DFR data divided into 4 groups based on potential for dermal contact

ODM: Occupational Postapplication Risk Assessment

- Group 1
 - Crops: alfalfa, clover, lettuce, mint
 - Activity: irrigating
- Group 2
 - Crops: ornamentals and turnips
 - Activities: sorting and packing
 - Crops: alfalfa, lettuce, mint
 - Activity: hand-harvesting

ODM: Occupational Postapplication Risk Assessment

- Group 3
 - Crops: low-growing vegetables, strawberries
 - Activities: hand-harvesting (also stake/tie or irrigating)
 - Crops: corn
 - Activities: stake/tie or irrigating

ODM: Occupational Postapplication Risk Assessment

- Group 4
 - Crops: fruit and nut trees
 - Activities: all activities (e.g., harvest, prune, rake, pole and pickup, and prop)
 - Crops: corn, turnips
 - Activity: hand- harvesting
 - Crops: ornamentals
 - Activities: transplanting or ball/burlapping

ODM: Occupational Postapplication Risk Assessment

Results

Crop	Rate (lb a.i./A)	Transfer Coefficient (cm ² /hr)	REI (MOE>100)
Cauliflower ¹	0.5	2,500	Day 6
Cotton	0.5	1,000	Day 5
Bell Pepper ²	0.5	4,000	Day 47
Sugar Beet	0.75	1,000	Day 59

Current REI is 48 hours

¹Represents all cole crops

²Also representative of eggplant

ODM: Occupational Postapplication Risk Assessment

Results

Crop	Rate (lb a.i./A)	Transfer Coefficient (cm ² /hr)	REI (MOE >100)
Group 1	0.56	1,000	Day 15
Group 2	0.56	2,500	Day 19
Group 3	0.56	4,000	Day 21
Group 4	0.56	10,000	Day 25

Current REI is 48 hours

ODM: Occupational Risk Assessment

Incident Reports

- Sources
 - OPP Incident Data System
 - Poison Control Centers, 1985-1996
 - California Department of Pesticide Regulation
 - National Pesticide Telecommunication Network
- Conclusion
 - Most risk is from use by pesticide handlers
 - ODM is not among the 10 highest rankings of hazard

Methidathion: Occupational Risk Assessment

Gary Bangs, Occupational Risk Assessor
Health Effects Division
OPP

Methidathion: Occupational Risk Assessments

Handlers

- Professional pesticide applicators and farmers/growers who mix, load and apply pesticides

Post-Application Workers

- Workers who irrigate, cultivate (weed/hoe), hand harvest, sort & pack, stake/tie or prop, transplant, scout

Methidathion: Occupational Handler Risk Assessments

Handler Risk Factors

- Formulation, activity, and application equipment
- Levels of protection
- Rate of application (lbs. ai/acre)
- Areas treated per day (e.g., acres/day)
- Dose and toxicity endpoint (mg/kg/day)

Methidathion: Occupational Handler Risk Assessments

Handler Risk

$$\text{Dose} = \frac{\text{UE} \times \text{App Rate} \times \text{Acres Treated}}{\text{Body Weight}}$$

$$\text{MOE} = \frac{\text{NOAEL}}{\text{Dose}}$$

Methidathion: Occupational Handler Risk Assessment

- Short-term exposure
 - Dermal dose:
 - NOAEL of 20 mg/kg/day
 - Inhalation dose:
 - NOAEL of 0.2 mg/kg/day
 - Target MOE: 100

Methidathion: Occupational Handler Risk Assessment

- Intermediate-term exposure
 - Dermal dose:
 - Less than 30 days: NOAEL of 20 mg/kg/day
 - Greater than 30 days: NOAEL of 0.2 mg/kg/day
 - Inhalation dose:
 - NOAEL of 0.2 mg/kg/day
 - Target MOE: 100

Methidathion: Occupational Handler Risk Assessments

Pesticide Handlers Exposure Database

- Developed by Task Force
- Monitored exposure data
- Consistency
- Widely accepted

Methidathion: Occupational Handler Risk Assessments

Handler Exposure Scenarios

- Mixer/Loader (M/L)
 - Mixing and loading wettable powder (WP) in soluble bag or emulsifiable concentrate (EC) for:
 - Aerial spraying
 - Groundboom spraying
 - Airblast spraying

Methidathion: Occupational Handler Risk Assessments

Handler Exposure Scenarios (cont.)

- Applicators (A)
 - Applying liquid via:
 - Aerial spraying
 - Groundboom spraying
 - Airblast spraying

Methidathion: Occupational Handler Risk Assessments

Handler Exposure Scenarios (cont.)

- Mixer/Loader/Applicator (M/L/A)
 - Mixing, loading and applying liquid using:
 - Low-pressure hand wand sprayer
 - Backpack sprayer
- Flagger (F)
 - Flagging of aerial liquid application

Methidathion: Occupational Handler Risk Assessments

Current EPA Label Requirement

- Long-sleeved shirt
- Long pants
- Waterproof gloves
- Shoes and socks
- Protective eyewear (for EC)
- Respirators appropriate for indoor and outdoor exposures

Methidathion: Occupational Handler Risk Assessments

Handler Exposure Control Levels

- Minimal protective equipment
 - **Single layer clothing***
 - **Waterproof gloves***
- Additional protective equipment (PPE)
 - Coveralls for dermal exposure
 - **Dust/mist respirator for inhalation exposure***

*Required on current label

Methidathion: Occupational Handler Risk Assessments

Handler Exposure Control Levels

- Engineering controls
 - Mixer/loaders: soluble bag for wettable powder or closed system for liquids
 - Applicators: enclosed cab tractor

Methidathion: Occupational Handler Risk Assessments

- Dermal exposure MOEs > 100
 - Minimal PPE: 7/12
 - Additional PPE: 8/12
 - Engineering controls: 11/12
- Mixer/loader for aerial:
 - With additional PPE: MOE = 45
 - With closed system: MOE = 91

Methidathion: Occupational Handler Risk Assessments

- Inhalation exposure MOEs > 100
 - Minimal PPE: 6/12
 - Additional PPE: 9/12
 - Engineering controls: 11/12
- Mixer/loader for aerial
 - With additional PPE: MOE = 33
 - With closed system: MOE = 95

Methidathion: Occupational Handler Risk Assessments

Additional protective measures required beyond current EPA labeling

- Mixing/loading WP in WSB for aerial: coveralls
- Mixing/loading liquid (EC) for aerial: enclosed system
- Airblast sprayer: enclosed cab
- Flagger for aerial: enclosed cab

Methidathion: Occupational Postapplication Risk Assessments

Postapplication Worker Risk Factors

- Dislodgeable Foliar Residue (DFR)
 - Amount of residue that workers could contact in field
- Transfer Coefficient (TC, cm^2/hour)
 - Indicator of amount that workers actually contact during various field activities

Methidathion: Occupational Postapplication Risk Assessments



Methidathion: Occupational Postapplication Risk Assessments

Postapplication Worker Risk Calculation

$$\text{Dose} = \frac{\text{DFR} \times \text{TC} \times \text{hours worked}}{\text{body weight}}$$

$$\text{MOE} = \frac{\text{NOAEL}}{\text{Dose}}$$

Methidathion: Occupational Postapplication Risk Assessments

Data Sources

- DFR study on cotton (California, North Carolina & Texas).
- DFR study on citrus (California & Florida)
- Surrogate DFR data for other crops (artichoke, kiwi, etc.)
- Transfer Coefficient
 - Standard values

Methidathion: Occupational Postapplication Risk Assessments

Postapplication Activities of Low Concern

- Dormant trees (no foliage)
- Mechanically harvested crops, e.g., cotton, safflower

Methidathion: Occupational Postapplication Risk Assessments

Current Re-entry Intervals (REIs) on labels

- **48 hours** at ≤ 2 lbs ai/acre per application
- **14 days** at > 2 lbs ai/acre per application

Methidathion: Occupational Postapplication Risk Assessments

Short-term Postapplication: Results

Crop	Activity	Rate lb ai/A	TC cm ² /hr	REI (MOE ≥ 100)
Cotton (NC)	Early scouting	1	1000	Day 1
	Late scouting	1	4000	Day 6
Cotton (TX)	Early scouting	1	1000	Day 1
	Late scouting	1	4000	Day 7
Safflower	Scouting	1	1000	Day 2
Kiwi, etc.	Cultivating	2	10,000	Day 17

*Dermal NOAEL = 20 mg/kg/day

Methidathion: Occupational Post-Application Risk Assessments

Intermediate-term Postapplication: Results

Crop	Activity	Rate lbs i/A	TC cm ² /hr	REI (MOE ≥ 100)
Citrus	Harvesting	2.8	10,000	Day 24
Artichoke	Harvesting	1	500	Day 15
Kiwi, etc.	Harvesting	2	10,000	Day 34

*Oral NOAEL = 0.2 mg/kg/day (30% dermal absorption)

Methidathion: Occupational Risk Assessments

Incident Reports

- The number of poisoning cases is small in relation to other organophosphate and carbamate pesticides.
- Methidathion was not on the list of top 20 chemicals in the National Pesticide Telecommunications Network (NPTN).

Methidathion: Occupational Risk Assessment

Data Gaps

- Handler assessment based on PHED
- Most postapplication scenarios extrapolated from 2 studies

Hazard Identification for Dietary Risk Assessment

Jess Rowland, Branch Chief
Health Effects Division
OPP

Dietary Risk Assessments

Acute

- Reflects one-day dietary exposures to pesticide residues

Chronic

- Reflects lifetime (long-term) exposures to pesticide residues

Expression of Dietary Risk

Reference Dose
(RfD)

$$\text{RfD} = \frac{\text{NOAEL}}{\text{UF}}$$

Expression of Dietary Risk

Population Adjusted Dose (PAD)

$$\text{PAD} = \frac{\text{RfD}}{\text{FQPA Safety Factor}}$$

$$\% \text{PAD} = \frac{\text{Exposure}}{\text{PAD}} \times 100$$

< 100% PAD is not of concern

ODM: Acute Hazard (Toxicity)

Dietary Endpoint Selection

- **Study:** acute neurotoxicity study in rats
- **Endpoint:** red blood cell (RBC) and brain cholinesterase inhibition
 - NOAEL: Not determined
 - LOAEL: 2.5 mg/kg/day
- Endpoints from this study most accurately reflect toxicity which could result from one-day dietary exposure to ODM

ODM: Chronic Hazard (Toxicity)

- **Study:** 1-year chronic toxicity study in dogs
- **Endpoint:** RBC and brain cholinesterase inhibition
 - **NOAEL:** 0.0125 mg/kg/day
 - **LOAEL:** 0.125 mg/kg/day
- Endpoints from this study most accurately reflect toxicity which could result from long-term dietary exposure to ODM.

ODM: Uncertainty Factors for Dietary Risk Assessment

- | | |
|-------|----------------------------|
| ● 10X | Interspecies Variability |
| ● 10X | Intraspecies Sensitivity |
| ● 1X | FQPA Safety Factor Removed |
| ● 3X | Lack of NOAEL (acute only) |
-

- | | |
|--------|-------------------|
| ● 300X | Total for Acute |
| ● 100X | Total for Chronic |

This would have been a typical type of uncertainty analysis, even before FQPA.

ODM: FQPA Assessment

- No developmental effects in fetuses below maternally toxic doses
- No increased sensitivity in pups relative to adults
- No abnormalities in developing fetal nervous system
- No histopathology of the nervous system

ODM: FQPA Assessment

- Complete toxicity database
- Exposure (dietary food and water) unlikely to underestimate exposure
- Based on the above weight-of-evidence considerations, the FQPA safety factor was removed for ODM risk assessments

ODM: Reference Doses

$$\text{Acute RfD: } \frac{2.5 \text{ mg/kg/day}}{300 \text{ (UF)}} = 0.008 \text{ mg/kg}$$

Chronic RfD:

$$\frac{0.0125 \text{ mg/kg/day}}{100 \text{ (UF)}} = 0.000125 \text{ mg/kg}$$

$$\% \text{RfD} = \frac{\text{Exposure}}{\text{RfD}} \times 100$$

Methidathion: Acute Hazard (Toxicity)

Dietary Endpoint Selection

- **Study:** Subchronic neurotoxicity in rats
- **Endpoint:** Plasma, RBC & brain cholinesterase inhibition
 - **NOAEL** = 0.2 mg/kg/day
 - **LOAEL** = 0.6 mg/kg/day
- Endpoint from this study most accurately reflects toxicity which could result from acute dietary exposure to methidathion

Methidathion: Chronic Hazard (Toxicity)

- **Study:** 1-year chronic toxicity in dogs
- **Endpoint:** RBC cholinesterase inhibition and liver toxicity
 - **NOAEL** = 0.15 mg/kg/day
 - **LOAEL** = 1.33 mg/kg/day
- Endpoint from this study most accurately reflects toxicity which could result from long-term dietary exposure to methidathion

Methidathion: Uncertainty Factors

- | | |
|--------|--|
| ● 10x | Interspecies Extrapolation |
| ● 10x | Intraspecies Variation |
| ● 1x | FQPA Safety Factor |
| <hr/> | |
| ● 100x | Total for acute and chronic dietary risk assessments |

This would have been a typical type of uncertainty analysis, even before FQPA

Methidathion: FQPA Assessment

- No developmental effects in fetuses below maternally toxic doses
- No increased sensitivity in pups relative to adults
- No abnormalities in developing fetal nervous system
- No histopathology of the nervous system

Methidathion: FQPA Assessment

- Complete toxicity database
- Exposure (dietary food and water) unlikely to underestimate exposure
- Based on the above weight-of-evidence considerations, the FQPA safety factor was removed for methidathion risk assessments

Methidathion: Reference Doses

$$\text{Acute RfD: } \frac{0.2 \text{ mg/kg/day}}{100 \text{ (UF)}} = 0.002 \text{ mg/kg}$$

$$\text{Chronic RfD: } \frac{0.15 \text{ mg/kg/day}}{100 \text{ (UF)}} = 0.0015 \text{ mg/kg}$$

Dietary Risk Assessments

Paula Deschamp, Risk Assessor
Health Effects Division
OPP

Dietary Risk Assessments

Acute

- Reflects one-day dietary exposures to pesticide residues

Chronic

- Reflects lifetime (long-term) exposures to pesticide residues

Dietary Risk Assessments

Dietary Exposure = Consumption x Residue

Risk = Hazard x Exposure

Exposure: Consumption

USDA's Continuing Survey of Food Intake
by Individuals (CSFII) 1989-91 Data

- 1-year surveys designed to measure what Americans eat and drink
- Represents the general population and subpopulations including infants and children

Exposure: Residue Data

- Field trial and processing data
 - Data used in establishing EPA tolerance levels
- Monitoring data
 - USDA's Pesticide Data Program (PDP) data
 - Statistically designed for dietary risk assessment
 - Prepared as in the home (e.g., washing and peeling)

Exposure: Residue Data

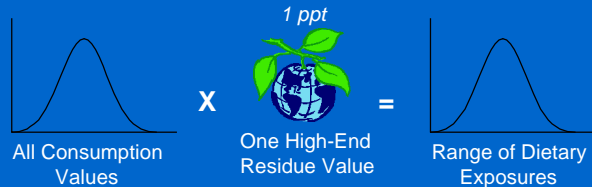
- Monitoring data (cont.)
 - FDA Surveillance Monitoring Data
 - Designed for tolerance enforcement
 - Large number of samples and types of food

Exposure: Residues

Tier	Residue Data Used
1	Tolerance level residues
2	Field trial residues
3	Monitoring data USDA PDP data FDA data

Two Types of Acute Dietary Risk Assessments

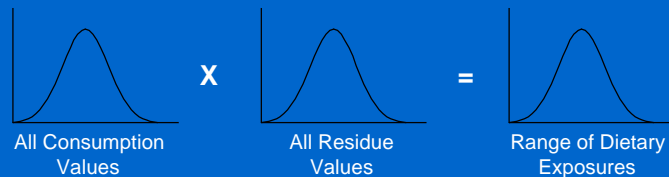
Non-Probabilistic



Assumes that every piece of fruit or vegetable consumed has residues at a high level. Therefore, a consumer's chance of consuming a high-residue piece of fruit or vegetable depends entirely on whether he or she eats that fruit or vegetable.

Two Types of Acute Dietary Risk Assessments (cont.)

Probabilistic



Assumes that any one piece of fruit or vegetable consumed can have residues anywhere in the range of residues observed. Therefore, a consumer's chance of consuming a high-residue piece of fruit or vegetable depends both on how much of the item he or she eats AND how frequently that item is found to have high residues.

More realistic exposure estimates.

Expression of Dietary Risk

$$RfD = \frac{NOAEL}{UF}$$

$$PAD = \frac{RfD}{FQPA \text{ Safety Factor}}$$

$$\%PAD = \frac{\text{Exposure} \times 100}{PAD}$$

<100% PAD not of concern

ODM: Dietary Risk Assessment

- Acute and Chronic Dietary Assessments
 - Tier 3 used monitoring and field trial data and incorporated information on percent of crop treated
- Acute Assessment
 - Tier 3 (probabilistic)
- Chronic Assessment
 - Tier 3 (non-probabilistic)

ODM: Residue Data Sources

- USDA Pesticide Data Program (PDP)
- FDA Surveillance Monitoring Data
- Field trial data
- Processing data
- Note: Monitoring data were translated to similar crops if the crops had similar use patterns (e.g., orange juice to lemon juice)

ODM: USDA PDP Data Used

- Green beans (canned and frozen)
- Milk
- Orange juice
- Pears (fresh, dried and juice)
 - No residues were detected in any samples

ODM: Other Data Used

- FDA
 - Brassica crops
 - Corn
 - Cucumber
 - Citrus
 - Lettuce
 - Onions
 - Pumpkins/squash
 - Watermelon
- Field Trials
 - Cottonseed
 - Eggplant/pepper
 - Mint
 - Safflower
 - Strawberry
 - Sugar beets
 - Walnuts/filberts
 - Meat/poultry

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ODM: Acute Population Adjusted Dose (aPAD)

- aPAD = 0.008 mg/kg/day, based on:
 - LOAEL of 2.5 mg/kg/day
 - Uncertainty factors:
 - 10x interspecies extrapolation
 - 10x intraspecies variability
 - 3x lack of a NOAEL
 - 1x FQPA Safety Factor

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ODM: Acute Dietary Analysis Results

Risk Estimates as a Percentage of the Acute PAD

Population	% aPAD @99.9 th Percentile
General U.S.	4
Females 13+/nursing	7
Infants < 1 year	4
Nursing infants <1	3
Non-nursing infants	2
Children 1-6	6
Children 7-12	5

Assessment was done using DEEM v6.87 (the Dietary Exposure Evaluation Model).

ODM: Chronic Population Adjusted Dose (cPAD)

- cPAD = 0.000125 mg/kg/day, based on:
 - NOAEL of 0.0125 mg/kg/day
 - Uncertainty factors:
 - 10x interspecies extrapolation
 - 10x intraspecies variability
 - 1x FQPA Safety Factor

ODM: Chronic Dietary Analysis Results

Risk Estimates as a Percentage of the Chronic PAD

Population	% cPAD
General U.S.	2
Infants < 1 year	4
Nursing infants	1
Non-nursing infants	5
Children 1-6	5
Children 7-12	3

Assessment was done using DEEM (the Dietary Exposure Evaluation Model).

ODM: Drinking Water Exposure Assessment

- Assessment was conducted because of ODM's use pattern and environmental fate profile.
- A drinking water assessment was conducted based on screening-level model estimates.
- ODM was used as a surrogate for ODMS.

ODM: Drinking Water Risk Assessment

- Methodology
 - Determined exposure to ODM in food first, then considered any remaining allowable exposure in drinking water.
- Acute Risk (*based on model estimate*) is:
 - 93% of the acute PAD after acute food exposure is considered.
- Chronic Risk (*based on model estimate*) is:
 - 95% of the chronic PAD after chronic food exposure is considered.

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ODM: Drinking Water Risk Conclusions

Acute and Chronic Risk

- Drinking water exposure based on model estimates did not exceed the amount of the acute or chronic PADs allocated for ground and surface water.
- Acute and chronic exposure to ODM in drinking water is not a concern.

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ODM: Aggregate Risk Assessment

- Includes exposures from various sources:
 - Food
 - Drinking water
 - Residential and other non-occupational
- No registered residential and non-occupational uses of ODM
- Aggregate risk assessment for ODM would include food and drinking water only.

ODM: Aggregate Risk Assessment Results

- Food exposure not of concern
- Drinking water exposure based on model is not of concern
- Aggregate acute and chronic dietary risk from food and water sources is not of concern.

Methidathion: Dietary Risk Assessment

- Acute and Chronic Dietary Assessments
 - Used monitoring and field trial data for most crops and incorporated information on percent of crop treated.
- Acute Assessment
 - Tier 3 (probabilistic)
- Chronic Assessment
 - Tier 2 (non-probabilistic)

Methidathion: Data Used for Acute Dietary Risk Assessment

- | | |
|---|---|
| ● USDA/PDP <ul style="list-style-type: none">• Apple juice• Citrus juices• Canned peaches | ● Field Trial <ul style="list-style-type: none">• Artichokes• Citrus• Pome fruits• Stone fruits• Tree nuts |
| ● Tolerance Level <ul style="list-style-type: none">• Carambola• Kiwi• Longan• Safflower/sunflower seed | <ul style="list-style-type: none">• Cottonseed oil• Safflower/sunflower oil |

Methidathion: Acute Population Adjusted Dose (aPAD)

- aPAD = 0.002 mg/kg/day, based on:
 - NOAEL of 0.2 mg/kg/day
 - Uncertainty factors:
 - 10x interspecies extrapolation
 - 10x intraspecies variability
 - 1x FQPA Safety Factor

Methidathion: Acute Dietary Analysis Results

Risk Estimates as a Percentage of the Acute PAD

Population	% aPAD at 99.9 th Percentile
General U.S.	16
Females 13+/nursing	14
Children 1-6	28
Nursing infants <1 year	64

Assessment was done using DEEM (the Dietary Exposure Evaluation Model).

Methidathion: Chronic Population Adjusted Dose (cPAD)

- cPAD = 0.0015 mg/kg/day, based on:
 - NOAEL of 0.15 mg/kg/day
 - Uncertainty factors:
 - 10x interspecies extrapolation
 - 10x intraspecies variability
 - 1x FQPA Safety Factor

Methidathion: Chronic Dietary Analysis Results

Risk Estimates as a Percentage of the Chronic PAD

Population	% cPAD
General U.S.	9
Females 13+/nursing	3
Children (1-6 years)	23
Non-nursing infants <1 year	12

Assessment was done using DRES (the Dietary Risk Evaluation System).

Methidathion: Drinking Water Risk Assessment

- Drinking water estimates were obtained from modeling and limited California monitoring data.
- Determined exposure in food first, then considered any remaining allowable exposure in drinking water.
- Example
 - For children 1-6 years, 23% of the chronic PAD is “used” from exposure to food....therefore,
 - Approximately 77% of the remaining chronic PAD is available for exposure through drinking water. ¹⁵¹

Methidathion: Drinking Water Risk Assessment Results

- The modeling estimates for drinking water did not exceed the amount of the acute and chronic PAD allocated for exposure from drinking water.
- Acute and chronic exposure to methidathion in drinking water is not a concern.
- Actual monitoring data supports model estimates.

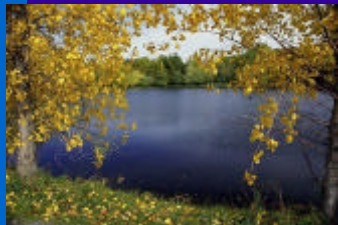
Methidathion: Aggregate Risk Assessment

- Acute and chronic aggregate risk assessment for methidathion would include food and drinking water.
 - Food exposure is not a concern.
 - Drinking water exposure is not a concern.
- No concern for acute or chronic aggregate risk due to exposure from food and drinking water.

Aggregate Risk Summary ODM and Methidathion

- Aggregate risk assessments included food and drinking water sources
- For each chemical alone, acute and chronic residue contributions in the diet of US population and infants and children are substantially below the Agency's level of risk concern.

Ecological Risk Assessment



Ecological Risk Assessments Overview

James Breithaupt, Agronomist
Environmental Fate and Effects Division
OPP

Environmental Risk Assessment

- Environmental Fate Assessment
 - Lab and field studies to characterize persistence and mobility
- Water Resources Assessment
 - Use monitoring and modeling to estimate potential exposure

Environmental Risk Assessment

- Ecological Toxicity
 - Acute and chronic tests to determine toxicity to terrestrial and aquatic organisms
- Ecological Risk Assessment
 - Compare exposure estimates to ecological toxicity to determine potential effects

Environmental Fate and Transport

Drinking Water Exposure Assessment

- Estimated Environmental Concentrations (EEC) from
 - SCI-GROW estimates upper limit ground water concentration
 - PRZM-EXAMS estimates upper limit surface water concentrations
- Methidathion - Refined with limited available monitoring data from
 - EPA's STORET and
 - California Public Drinking Water Sources

ODM: Environmental Fate Assessment

- Fate and Transport
 - Parent ODM and OP residues are non-persistent.
 - Non-OP residues appear to be persistent.
 - OP residues are the only residues of concern for human health.

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ODM: Environmental Fate Assessment

- Major Routes of Dissipation
 - Microbial metabolism in soil (half-life ~ 3 days)
 - Anaerobic aquatic metabolism (half-life ~ 3 days)
 - Other routes (half-lives ~ 40-137 days)
 - Non-persistent
- Mobility
 - All residues (parent and metabolites) are very mobile (K_d : 0.01-0.89 mL/g)

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ODM: Surface Water Exposure Assessment

- Even with maximum application rates and high exposure scenarios, drinking water exposure from surface water was not of concern for human health.
- No further refinement was necessary.

ODM: Ground Water Exposure Assessment

Based on SCI-GROW modeling and limited persistence in soil, ODM is not expected to reach ground water.

Methidathion: Environmental Fate Assessment

- Major Routes of Dissipation
 - Microbial metabolism in soil (half-life ~ 10 days)
 - Hydrolysis (half-life ~ 25 days @ pH 7)
 - Photodegradation on soil (half-life ~ 40 days)
 - Direct photolysis in water (half-life ~ 10 days)
 - Aquatic metabolism data not available
 - Moderately persistent
- Mobility
 - Moderately mobile (kd: 2.5 ~ 14.8 mL/g)

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Methidathion: Water Exposure Assessment

- Tier 2 PRZM-EXAMS scenarios with high EEC potential and regional-specific use rates
- Monitoring data support the modeling results
- SCI-GROW used for groundwater EECs
- Drinking water concentrations are below the level of concern for human health

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Ecological Effects

Dan Rieder, Biologist
Environmental Fate and Effects Division
OPP

Ecological Effects Overview

- Toxicity information used to assess risk to terrestrial and aquatic organisms
 - Birds, acute and chronic
 - Mammals, acute and chronic
 - Fish and invertebrate, acute and chronic
- Toxicity categories
 - Useful for ranking chemicals and discussing relative toxicity
 - Not sole basis for risk conclusions

Ecological Risk Assessment

Toxicity and Exposure

- **Risk Quotient (RQ):** Ratio of estimated exposure concentration to toxicity endpoint

$$\text{Acute RQ} = \frac{\text{Peak environmental concentration}}{\text{LD}_{50}, \text{LC}_{50}, \text{ or } \text{EC}_{50}}$$

$$\text{Chronic RQ} = \frac{\text{Long-term average concentration}}{\text{NOAEC or LOAEC}}$$

RQ is compared to Levels of Concern (LOC)
The lower the RQ, the lower the risk

ODM: Ecological Risk Assessment

Avian

- Acute risk is low
- Chronic risk is high
 - Reduction in number of surviving embryos
 - Reduction in body weight of young

...

ODM: Ecological Risk Assessment

Mammals

- Low acute risk
- High chronic risk
 - Based on rat reproduction study

Insects

- Highly toxic to honey bees

...

ODM: Ecological Risk Assessment

Aquatic

- Low risk to freshwater fish
- Low risk to freshwater invertebrates
- Exposure much lower than toxicity
- Insufficient data to assess estuarine and marine animals

ODM: Summary of Ecological Risk

- Low acute risk to birds and mammals
- Low risk to aquatic organisms
- Possible chronic effects to birds and mammals

Methidathion: Ecological Risk Assessment

Avian

- All uses
 - High acute risk
 - Very high chronic risk to birds
 - Based on maximum and typical rates
 - Long-term residues exceed chronic toxicity threshold of concern

Methidathion: Ecological Risk Assessment

Avian (cont.)

- Avian reproduction study with mallards
 - NOAEL = 1 ppm; LOAEL = 10 ppm
 - Significant effects:
 - Increased numbers of cracked eggs
 - Reduced numbers of hatchlings
- A second test indicates
 - NOAEL = 30 ppm; highest level tested

Methidathion: Incidents

- 5 incidents: methidathion detected in or on bird of prey carcasses
- In 2 of those incidents: methidathion contributed to mortality

Methidathion: Ecological Risk Assessment

Mammals

- High acute risk
- Very high chronic risk
- Based on maximum and typical rates
- Long-term residues exceed chronic toxicity threshold of concern

Methidathion: Ecological Risk Assessment

Mammals (cont.)

- Two studies:
 - NOAEL ~ 5 ppm; LOAEL ~ 25 and 32 ppm
 - Significant effects:
 - Decreased mating index
 - Decreased pup weight

Insects

- Highly toxic to honey bees

Methidathion: Ecological Risk Assessment

Aquatic

- High acute and chronic risk to fish and invertebrates
- Chronic aquatic risk
 - Based on maximum and typical rates
 - Based on long-term average concentrations
 - Includes modeling of California use patterns and sites

Methidathion: Ecological Risk Assessment

Aquatic (cont.)

- Chronic effects
 - Fish: reduced survival of fry after hatch and reduced growth
 - Invertebrates: reduced survival, reduced number of young
- Risk to estuarine species minimal
- Significant estuarine exposure unlikely in California

Methidathion: Summary of Ecological Risk

- Maximum and regional-specific application rates assessed
 - All uses represent risks of concern to terrestrial and aquatic animals
- Greatest risk is of chronic effects (birds and aquatic invertebrates)
 - Based on long-term average dietary exposure
 - For aquatic organisms, included risk based on California use patterns and sites

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Discussion of Refinement of Risk Assessment

- A very critical factor is the extreme chronic toxicity to birds, mammals, and aquatic invertebrates.
- Monitored aquatic residues in some cases support estimated concentrations.

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Risk Summary & Next Steps

Kathleen Meier, Chemical Review Manager
Special Review and Reregistration Division
OPP

ODM: Risk Summary

- Dietary
 - No risk concern for food and drinking water
- Worker
 - High risk for handlers
 - Mixing, loading, applying for most intermediate-term scenarios (>7 days)
 - Postapplication
 - REIs from 5-59 days
- Ecological
 - High chronic risk to birds, mammals, honey bees

Methidathion: Risk Summary

- Dietary
 - No risk concern for food and drinking water
- Worker
 - Handler
 - Risks mitigated with additional PPE and engineering controls
 - Postapplication
 - REIs from 1-34 days (24 citrus)
- Ecological
 - High acute and chronic risk to birds, mammals, aquatic species

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Risk Mitigation

Worker risk

- Mitigation
 - Lower application rates
 - Extend intervals between applications
 - Remove highest risk application methods
- Risk refinement
 - New data or use information

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Risk Mitigation

Ecological risk

- Lower application rates
- Extend intervals between applications
- Buffer zones for methidathion

Next Steps

- 60-day public comment period
- E-mail comments to:
 - opp-docket@epa.gov
- Mail comments to:
 - U.S. EPA
OP Pesticide Docket (7502C)
401 M St. SW
Washington, DC 20460

Contacts

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Methidathion

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